

ABSTRACT OF THE DISCLOSURE

The present invention relates to a method of selecting a protein variant having reduced immunogenicity as compared with the parent protein. This method includes the steps of screening a random peptide
5 display package library with antibodies raised against any protein of interest, sequencing the amino acid sequence of the antibody binding peptides, or the DNA sequence encoding the antibody binding peptides, identifying epitope patterns of a protein by sequence alignment of the reactive peptide sequence, localization of epitope patterns on the
10 primary 3-dimensional structure of the parent protein, defining an epitope area including amino acids situated within 5 Å from the epitope amino acids, and affecting antibody binding to the epitope, changing the localized epitope patterns, or amino acids defining the epitope area of the parent protein by genetic engineering mutations of
15 a DNA sequence encoding the parent protein without impairing functionality of the protein using the emerging epitope database for eliminating amino acid substitutions creating new or duplicating existing epitope patterns, introducing the mutated DNA sequence into a suitable host, culturing the host and expressing the protein variant,
20 and evaluating the immunogenicity of the protein variant using the parent protein as reference. The invention further relates to the protein variant and its use, as well as to a method for producing said protein variant.